REMARKS

Claims 12-29 were previously deleted. Claim 1 has been amended to more clearly describe that the removal of solvent in the hydrophilic membrane results in a hydratable matrix. Support for the amendment can be found in the application, for example, on page 13. No new matter is added. Claims 2, 3, and 4 are amended to make the language flow better. Support for the amendment can be found throughout the application and the originally filed claims. No new matter is added. New claims 30 and 31 are added to address moisture content of the hydratable matrix after drying. Support for the new claims can be found in the specification, for example, on page 13, paragraph 36. No new matter is added. New claim 32 addresses placing a hydrating material layer either between the electrode and the hydratable agent-containing matrix or on the body surface proximal side of the hydratable agent-containing matrix. Support for the new claim can be found in the specification, for example, in the originally filed claims. No new matter is added. New claim 33 addresses a method making an anhydrous layer involving dissolving in an aqueous solvent and removing the solvent to result in a hydratable matrix of certain thickness and moisture and placing a hydrating material layer either between the electrode and the hydratable agent-containing matrix or on the body surface proximal side of the hydratable agent-containing matrix. Support for the new claims can be found in the specification, for example, on page 13, paragraph 36 and page 14, paragraph 39 and in the original claims. No new matter is added. Claims 1-11 and 30-33 are pending.

The specification has been amended to correct spelling of a word and to insert "μ" to correct clerical errors. Support for the new claim can be found in the specification, for example, in the originally filed claims. No new matter is added.

35 USC §103 Rejection

The Examiner rejected claims 1-2 and 5-11 under 35 USC 103 as being unpatentable over Haak et al. USPN 5,993,435. Insofar as the rejection is maintained over the amended claims, Applicant respectfully traverses the rejection.

The Examiner asserted that since the reservoir layer and filtration membrane of Haak are solvent-cast, a solvent must [be] present in the reservoir layer of Haak and since Haak teaches an anhydrous reservoir layer, the solvent of Haak must [be] inherently removed from the filtration membrane after casting. Applicant disagrees respectfully. First, Haak et al. did not teach or suggest a reservoir layer with a beneficial agent and hydrophilic polymer membrane, much less forming such a reservoir by dissolving the beneficial agent in a solvent, applying the solution to the hydrophilic polymer membrane and removing solvent. Haak et al. taught having a selective membrane ***separating*** a reservoir layer and an electrolyte layer wherein the membrane will selectively allowing only ions of selected molecular size to pass. This is entirely different from the present invention in which the reservoir layer has both the filtration membrane and the beneficial agent.

Further, regarding the present claims that relate to aqueous based solvent, Haak et al. failed to teach or suggest dissolving a beneficial agent in an aqueous solvent before casting the material on a hydrophilic membrane. The Examiner asserted that both reservoir layer and filtration membrane of Haak are solvent-cast (Example 1). However, in Example 1 of Haak et al. only the permeable membrane was solvent cast and the solvent used was non-aqueous, i.e., it was methylene chloride. Furthermore, the electrolyte reservoir and the drug reservoir of Haak et al. in Example 1 were ***dry blended and extruded*** (column 16, lines 13-26). Haak et al. never taught or suggested using an aqueous medium for solvent casting a layer with the beneficial agent. In fact, Haak et al. taught against exposure to water. Haak et al. repeatedly warned that the reservoir layer and the electrolyte layer, and also the permeable membrane should be in a substantially dry condition (e.g., column 4, line 63-66, column 5, lines 49-51, column 11, lines 53-54, column 12, lines 53-55) before use. With the emphasis on being substantially dry before use and without any specific teaching on dissolving a beneficial agent in an aqueous based solvent, Haak et al. implied that water should be avoided before use on the skin. It is contrary to common sense to think that Haak et al. suggested dissolving the beneficial agent in an aqueous based solvent before use when Haak et al. in fact stressed the importance of maintaining dryness before use.

The Examiner (quoting col. 11, line 53 and col 13, lines 1-5 of Haak et al.) asserted that a solvent must be present, such as water or non-aqueous solvent. However, contrary to the

Examiner's assertion, in col. 11, line 53, Haak et al. actually stated that the layers be "maintained in a substantially non-hydrated condition until use." Certainly this is not teaching or suggestion that an aqueous based solvent be used to dissolve the beneficial agent. Based on Haak et al.'s description of what it means to be substantially dry as inhibiting the passage of low molecular weight agent ions, a person skilled in the art would understand that Haak et al. were warning about water and giving a hint that not more than a trace amount of water is permissible, whatever the cause (perhaps contamination, moisture, although Haak et al did not describe). It certainly is not teaching that water should be used as a solvent for dissolving the beneficial agent before use. Regarding col. 13, lines 1-5, in context, Haak et al. were again talking about keeping the device non-hydrated until use and specifically stating that "there is insufficient solvent contained in the membrane to allow ionic species to become dissolved in the solvent and transported across the membrane." (col. 12, lines 61-67). Following that, Haak et al. only mentioned water in col. 13, lines 1-5 in the context of what it means to be hydrated. Hydration is only talked about in the context of putting the device in use on the body. For example, col. 12, line 63-67 stated that the "permeable membrane must be maintained in a substantially non-hydrated condition until placement on the body." Obviously the hydration is done when the device is placed on the body. This certainly is not a teaching or suggestion that water be used to dissolve the beneficial agent to make the reservoir layers.

Warning to stay substantially dry is certainly not teaching to get really wet and then try to get dried. Such an assertion would be, by analogy, just like asserting that a warning to not breathe in dust is a suggestion to inhale a lot of dust and then try to get rid of the dust from one's lungs. Dust, like moisture, is everywhere and hard to avoid, a warning about overexposure is surely not a suggestion to immerse into the substance. The Examiner asserted that solvent removal is equivalent to the drying step of the claimed invention. Again, there is no suggestion by Haak et al. to dissolve the beneficial agent in an aqueous based solvent and then drying to remove the solvent. Even if, for argument's sake, one assumed that Haak et al. suggests using a solvent to dissolve the beneficial agent, from the teaching of Haak et al. as whole, one would be led to use a non-aqueous solvent, such as methylene chloride. One would not be led to use an aqueous based solvent, for fear of going against the Haak et al. "substantially dry" teaching.

The Examiner also rejected claims 3-4 as being unpatentable over Haak in view of Huntington (6,057,374). Applicant respectfully traverses the rejection.

First, just as Haak et al. failed to teach forming a reservoir with a filtration membrane, Huntington also did not disclose using a filtration membrane with beneficial agent to form a matrix in a reservoir layer. Huntington only mentioned biological membranes (such as mucous membrane, etc.) which are entirely unrelated to filtration membranes. The only other membrane mentioned by Huntington is flux controlling membrane 30, which separates the reservoir 16 and body surface 100. Again, such a flux controlling membrane is not used in a reservoir, but rather it separates and controls ion movement from the reservoir. Thus, Huntington did not teach forming a beneficial agent containing reservoir with a filtration membrane, much less by a process of dissolving the beneficial agent in a solvent and removing the solvent.

The Examiner quoted Huntington (col. 3, line 54; col. 10, line 42; claim 12) and asserted that Huntington taught solvent casting with permeation enhancers such as ethanol in water. Applicant disagrees and respectfully requests the Examiner to read the passages in context. It is noted that ethanol is used by Huntington as a solvent for 1,2-dodecane diol for permeation enhancing (col, 13, lines 50-51). Regarding the use of permeation enhancers, they are to be added in such as way that cannot act as a solvent for the drug, but only in relatively dry form or just prior to use on the body. Huntington stated, in col. 5 line 62 to col. 6, line 6, "The permeation enhancers of the present invention may be incorporated into the hydratable reservoir of the donor and/or counter reservoirs of such devices in solid form at room temperature. This allows maintenance of the reservoir in a substantially liquid-free state during storage and handling. Alternatively, the permeation enhancer may be incorporated into the hydrating liquid which is added to the dry state reservoir just prior to use of the device. In either case, the permeation enhancer in liquid form does not contact device components such as metallic electrodes and silicone adhesives until just prior to use of the device." Thus, alcohol, when used, is to be added only in the context of keeping the reservoir liquid free or just prior to use. This is entirely unrelated to a step of adding alcohol to dissolve the beneficial agent to make a reservoir layer.

Regarding the language quoted by the Examiner, Huntington in col. 3, line 54 actually stated, "Most preferably, the reservoir is substantially nonhydrated until the time of use." This certainly is a teaching against getting exposed to too much water before use. Together with the above quoted language on the permeation enhancer use and preference on dry state, one skilled in the art will understand that in fact liquid form is not desirable. By no means can this statement be stretched to become a suggestion to dissolve the beneficial agent in a solvent and then removing the excess solvent, much less dissolving in an aqueous based solvent and removing the aqueous solvent. In col. 10, line 42, Huntington merely mentioned solvent casting along with melt blending and extrusion. Solvent casting does no necessarily mean dissolving a beneficial agent in the solvent first. The material to be cast can contain suspended drug particulates. Further, the quoted language certainly is not a teaching or suggestion about specifically dissolving in an aqueous based solvent or an alcohol. Furthermore, there is absolutely no mention of any filtration membrane forming a matrix in a reservoir layer.

Regarding claim 12, it depends on claim 9, which depends on claim 1, meaning that the aqueous solution of claim 12 involves using ethanol in the context of permeation enhancer and wherein the donor reservoir is ***substantially non-hydrated*** until the device is to be placed in operation. Again, referring to the aboved quoted Huntington language on permeation enhancers use in dry state composition, a skilled person will understand that Huntington did not teach dissolving the beneficial agent in liquid solvent before just prior to use, and especially did not teach using water or alcohol for dissolving the beneficial agent to make the matrix in a reservoir layer before use. If anything, in fact Huntington teaches against dissolving a beneficial agent in a liquid, and especially against dissolving in an aqueous based solvent.

The Examiner further asserted that, based on the teaching of Huntington on ethanol, isopropanol can obviously be used as a solvent. Applicant submits that ethanol was not used by Huntington as a solvent for the beneficial agent. Ethanol was used by Huntington as a solvent for 1,2-dodecane diol for permeation enhancing. Isopropanol may not perform well enough as a solvent for 1,2-dodecane diol. Regardless, according to Huntington, liquid form is to be avoided.

As mentioned in the specification of the present application, one problem with prior art devices is the difference in swelling properties of the hydrophilic reservoir and the electrode leading

to shearing along the contact surface, resulting in inoperative devices. Applicant has discovered that the present invention of dissolving the ingredients in a solvent, applying the solution on a hydrophilic filtration membrane and removing solvent can result in a stable reservoir which can be put in a device to afford extended shelf life (page 7 of the specification). There is no teaching or suggestion by either Haak et al. or Huntington that such a technique be used. There is only warning by both references that the layers be maintained substantially dry, avoiding liquid form, before use. There is absolutely no hint that the beneficial agent should or be dissolved in a solvent, much less in alcohol or an aqueous based solvent before being disposing on a filtration membrane to result in a desirable device.

Even if one were to make the unlikely assumption that one would try to dissolve the beneficial agent in a solvent before applying on a filtration membrane, there is no assurance that after solvent removal the device will be operational and stable without shearing on the electrode surface. Reasonable expectation of success is needed for a prima facie obviousness rejection based on modification or combination of prior art. See In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 374 (Fed. Cir. 1986). With the warning of Haak et al. and Huntington to keep the reservoir layer substantially dry just prior to use, one would not even want to try.

Thus, either alone or in combination, Haak et al. and Huntington do not render the presently claimed invention obvious. Withdrawal of the rejections is respectfully requested.

It is further submited that in the dependent claims are additional nonobvious features over the prior art. For example, in a drying step, water is removed so that 1% or less (in another case, 5% or less) of residual moisture is in the matrix. There is no indication in the prior art that such low moisture matrix can be used in a device and can avoid prior art problems of shearing between reservoir layer and electrode and not result in device failure.

CONCLUSION

Applicant submits the pending claims are novel and nonobvious over prior art and comply with the requirements of 35 USC 112. The examination and passage to allowance of the pending claims are respectfully requested. An early Notice of Allowance is therefore earnestly solicited. Applicant invite the Examiner to contact the undersigned at (650) 564-7054 to clarify any unresolved issues raised by this response.

Respectfully submitted,

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